

## PATENT COOPERATION TREATY

09/719604

PCT

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

BILLINGS, Lucy, J.  
Incyte Pharmaceuticals, Inc.  
3174 Porter Drive  
Palo Alto, CA 94304  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 10 October 2001 (10.10.01)	
Applicant's or agent's file reference PF-0544 PCT	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/US99/14711	International filing date (day/month/year) 29 June 1999 (29.06.99)
International publication date (day/month/year) 06 January 2000 (06.01.00)	Priority date (day/month/year) 30 June 1998 (30.06.98)
Applicant INCYTE PHARMACEUTICALS, INC. et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
30 June 1998 (30.06.98)	60/091,177	US	02 Sept 1999 (02.09.99)
16 July 1998 (16.07.98)	60/155,241	US	17 July 2001 (17.07.01)

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

PETRESKA Gorica

Telephone No. (41-22) 338.83.38

## P. ENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 12 April 2000 (12.04.00)	
<b>International application No.</b> PCT/US99/14711	<b>Applicant's or agent's file reference</b> PF-0544 PCT
<b>International filing date (day/month/year)</b> 29 June 1999 (29.06.99)	<b>Priority date (day/month/year)</b> 30 June 1998 (30.06.98)
<b>Applicant</b> BANDMAN, Olga et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
26 January 2000 (26.01.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

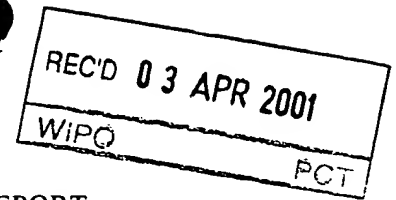
<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer Nestor Santesso</p> <p>Telephone No.: (41-22) 338.83.38</p>
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



14

Applicant's or agent's file reference PF-0544 PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/14711	International filing date (day/month/year) 29 JUNE 1999	Priority date (day/month/year) 30 JUNE 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/53, 9/02; C12Q 1/68; A61K 38/44 and US Cl. 435/189; 424/94.4; 530/189;		
Applicant INCYTE PHARMACEUTICALS, INC		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  26 JANUARY 2000	Date of completion of this report  15 DECEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  PADMA BASKAR  TERRY J. DEY PARALEGAL SPECIALIST TECHNOLOGY CENTER 1600
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1600

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/14711

**I. Basis of the report**1. With regard to the **elements** of the international application: \*☐ the international application as originally filed☒ the description:pages 1-64

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of \_\_\_\_\_

☒ the claims:pages 65-66

, as originally filed

pages NONE

, as amended (together with any statement) under Article 19

pages NONE

, filed with the demand

pages NONE

, filed with the letter of \_\_\_\_\_

☒ the drawings:pages 1-5

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:pages NONE

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/Fig NONE5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/14711

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. statement

Novelty (N)	Claims <u>1-20</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-20</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-20</u>	YES
	Claims <u>NONE</u>	NO

## 2. citations and explanations (Rule 70.7)

Claims 1-20 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the human oxidoreductase proteins (HORP) and polynucleotides which identify and encode HORP. Furthermore, the prior art does not teach or suggests antibodies, agonists, antagonists, methods for diagnosing, treating or preventing disorders associated with human oxidoreductase proteins.

----- NEW CITATIONS -----  
NONE

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>C12N 15/53, 9/02, C12Q 1/68, C07K 16/40, A61K 38/44</b>		<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 00/00622</b>
			<b>(43) International Publication Date:</b> 6 January 2000 (06.01.00)
<b>(21) International Application Number:</b> PCT/US99/14711			<b>(US).</b> LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). GORGONE, Gina, A. [US/US]; 1253 Pinecrest Drive, Boulder Creek, CA 95006 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US).
<b>(22) International Filing Date:</b> 29 June 1999 (29.06.99)			
<b>(30) Priority Data:</b> 60/091,177 30 June 1998 (30.06.98) US 60/155,241 16 July 1998 (16.07.98) US			
<b>(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications</b> US 60/091,177 (CIP) Filed on 30 June 1998 (30.06.98) US 60/155,241 (CIP) Filed on 16 July 1998 (16.07.98)			
<b>(71) Applicant (for all designated States except US):</b> INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US).			
<b>(72) Inventors; and</b>			<b>(74) Agents:</b> BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).
<b>(75) Inventors/Applicants (for US only):</b> BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View, CA 94040 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118			
			<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
			<b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
			<b>(88) Date of publication of the international search report:</b> 20 April 2000 (20.04.00)
<b>(54) Title:</b> HUMAN OXIDOREDUCTASE PROTEINS			
<b>(57) Abstract</b>  The invention provides human oxidoreductase proteins (HORP) and polynucleotides which identify and encode HORP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of HORP.			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
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AU	Australia	GA	Gabon	LV	Larvia	SZ	Swaziland
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DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/14711

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/53 C12N9/02 C12Q1/68 C07K16/40 A61K38/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GRIGORYEV, S. ET AL.: "A mouse amidase specific for N-terminal asparaginase - the gene, the enzyme, and their function in the N-end rule pathway." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 45, 8 November 1996, pages 28521-32, XP002116471 see the whole document ---	1-20
Y	DATABASE EMBL - EMBEST26 Entry HSC8355, Acc.no. C05835, 25 August 1996 TAKEDA, J.: "similar to N-terminal asparagine amidohydrolase." XP002119909 see the whole document --- -/--	1-20

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

25 October 1999

Date of mailing of the international search report

22.02.2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Smalt, R



## INTERNATIONAL SEARCH REPORT

Intern al Application No

PCT/US 99/14711

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMBEST2 Entry/Acc.no. AA715017, 19 January 1998 STRAUSBERG, R.: "nx94a04.s1 NCI CGAP GCB1 Homo sapiens cDNA clone IMAGE:1269870." XP002119910 see the whole document</p>	3-9,19, 20
X	<p>--- DATABASE EMBL - EMBEST2 Entry/Acc.no. Aa745642, 19 January 1998 STRAUSBERG, R. ET AL.: "ny69g04.s1 NCI CGAP GCB1 Homo sapiens cDNA clone IMAGE:1283574." XP002119911 see the whole document</p>	3-9,19, 20
A	<p>--- STEWART, A.E. ET AL.: "The sequence of porcine protein NH2-terminal asparagine amidohydrolase a new component of the N-end rule pathway." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 1, 6 January 1995, pages 25-8, XP002116472 see the whole document</p>	
A	<p>--- WO 98 20137 A (HAWKINS PHILLIPS R ;HILLMAN JENNIFER L (US); INCTYE PHARMACEUTICAL) 14 May 1998 see claims see the whole document</p>	
A	<p>--- EP 0 712 932 A (SUMITOMO CHEMICAL CO) 22 May 1996</p>	
A	<p>--- DATABASE BIOSIS BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US Acc.no. 1987:211958, 1986 CLAUSEN, N. ET AL.: "Determination of L-asparagine activity in serum by thin-layer chromatography application to the treatment of acute lymphoblastic leukemia." XP002119912 see abstract</p> <p>-----</p>	17

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 14711

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 17 and 18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
  
1-20 (partially), see additional sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 99/14711

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 3.

Further defect(s) under Article 17(2)(a):

Claims 15, 16 and 18 could not be searched to completion due to insufficient characterization of the (ant)agonists in the description.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 99/14711

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-20, all partially

The human oxidoreductase designated HORP1, as defined by sequence ID's 1 and 7, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

2. Claims: 1-20, all partially

The human oxidoreductase designated HORP2, as defined by sequence ID's 2 and 8, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

3. Claims: 1-20, all patially

The human oxidoreductase designated HORP3, as defined by sequence ID's 3 and 9, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

4. Claims: 1-20, all partially

The human oxidoreductase designated HORP4, as defined by sequence ID's 4 and 10, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

5. Claims: 1-20, all partially

The human oxidoreductase designated HORP5, as defined by sequence ID's 5 and 11, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 99/14711

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

nucleic acid in a sample, optionally involving amplification.

## 6. Claims: 1-20, all partially

The human oxidoreductase designated HORP6, as defined by sequence ID's 6 and 12, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/14711

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9820137 A	14-05-1998	US 5861496 A	19-01-1999
		AU 5585898 A	29-05-1998
		EP 0941342 A	15-09-1999
EP 0712932 A	22-05-1996	JP 8140674 A	04-06-1996
		CA 2163136 A	19-05-1996
		US 5928921 A	27-07-1999
		US 5942426 A	24-08-1999

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PF-0544 PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 14711</b>	International filing date (day/month/year) <b>29/06/1999</b>	(Earliest) Priority Date (day/month/year) <b>30/06/1998</b>
Applicant <b>INCYTE PHARMACEUTICALS, INC. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 14711

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 17 and 18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-20 (partially), see additional sheet, subject 1.

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box 3.

Further defect(s) under Article 17(2)(a):

Claims 15, 16 and 18 could not be searched to completion due to insufficient characterization of the (ant)agonists in the description.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-20, all partially

The human oxidoreductase designated HORP1, as defined by sequence ID's 1 and 7, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

2. Claims: 1-20, all partially

The human oxidoreductase designated HORP2, as defined by sequence ID's 2 and 8, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

3. Claims: 1-20, all patially

The human oxidoreductase designated HORP3, as defined by sequence ID's 3 and 9, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

4. Claims: 1-20, all partially

The human oxidoreductase designated HORP4, as defined by sequence ID's 4 and 10, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

5. Claims: 1-20, all partially

The human oxidoreductase designated HORP5, as defined by sequence ID's 5 and 11, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

nucleic acid in a sample, optionally involving amplification.

6. Claims: 1-20, all partially

The human oxidoreductase designated H0RP6, as defined by sequence ID's 6 and 12, nucleic acids encoding it, variants of said protein/nucleic acid, expression vector, host cell, method for producing the protein using said host, antibody, (ant)agonist, pharmaceutical composition comprising said protein or antagonist, and methods for detecting said nucleic acid in a sample, optionally involving amplification.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/14711

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/53 C12N9/02 C12Q1/68 C07K16/40 A61K38/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GRIGORYEV, S. ET AL.: "A mouse amidase specific for N-terminal asparaginase - the gene, the enzyme, and their function in the N-end rule pathway." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 45, 8 November 1996, pages 28521-32, XP002116471 see the whole document ---	1-20
Y	DATABASE EMBL - EMBEST6 Entry HSC8355, Acc.no. C05835, 25 August 1996 TAKEDA, J.: "similar to N-terminal asparagine amidohydrolase." XP002119909 see the whole document --- -/-	1-20

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## ° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

25 October 1999

Date of mailing of the international search report

22.02.2000

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/14711

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMBEST2  Entry/Acc.no. AA715017, 19 January 1998  STRAUSBERG, R.: "nx94a04.s1 NCI CGAP GCB1  Homo sapiens cDNA clone IMAGE:1269870."  XP002119910  see the whole document</p> <p>---</p>	3-9, 19, 20
X	<p>DATABASE EMBL - EMBEST2  Entry/Acc.no. Aa745642, 19 January 1998  STRAUSBERG, R. ET AL.: "ny69g04.s1  NCI CGAP GCB1 Homo sapiens cDNA clone  IMAGE:1283574."  XP002119911  see the whole document</p> <p>---</p>	3-9, 19, 20
A	<p>STEWART, A.E. ET AL.: "The sequence of  porcine protein NH2-terminal asparagine  amidohydrolase a new component of the  N-end rule pathway."  JOURNAL OF BIOLOGICAL CHEMISTRY,  vol. 270, no. 1, 6 January 1995,  pages 25-8, XP002116472  see the whole document</p> <p>---</p>	
A	<p>WO 98 20137 A (HAWKINS PHILLIPS R ;HILLMAN  JENNIFER L (US); INCTYE PHARMACEUTICAL) 14  May 1998  see claims  see the whole document</p> <p>---</p>	
A	<p>EP 0 712 932 A (SUMITOMO CHEMICAL CO) 22  May 1996</p> <p>---</p>	
A	<p>DATABASE BIOSIS  BIOSCIENCES INFORMATION SERVICE,  PHILADELPHIA, PA, US  Acc.no. 1987:211958, 1986  CLAUSEN, N. ET AL.: "Determination of  L-asparagine activity in serum by  thin-layer chromatography application to  the treatment of acute lymphoblastic  leukemia."  XP002119912  see abstract</p> <p>-----</p>	17

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/14711

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9820137 A	14-05-1998	US 5861496 A	19-01-1999
		AU 5585898 A	29-05-1998
		EP 0941342 A	15-09-1999
EP 0712932 A	22-05-1996	JP 8140674 A	04-06-1996
		CA 2163136 A	19-05-1996
		US 5928921 A	27-07-1999
		US 5942426 A	24-08-1999